

+

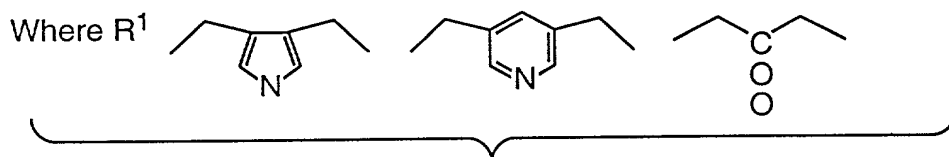
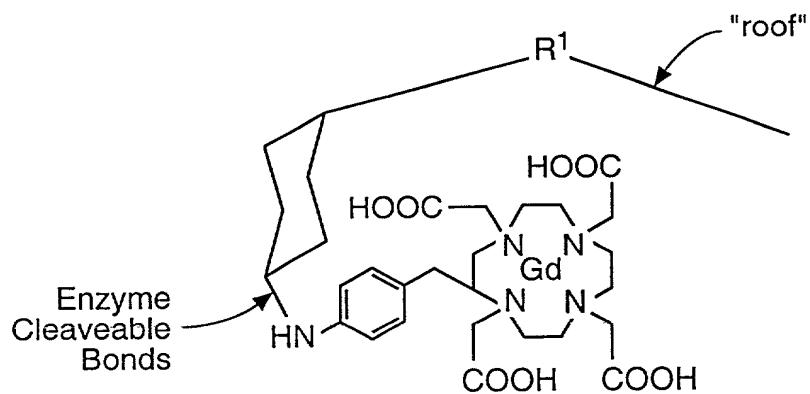


FIG._1

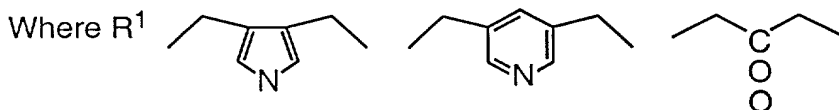
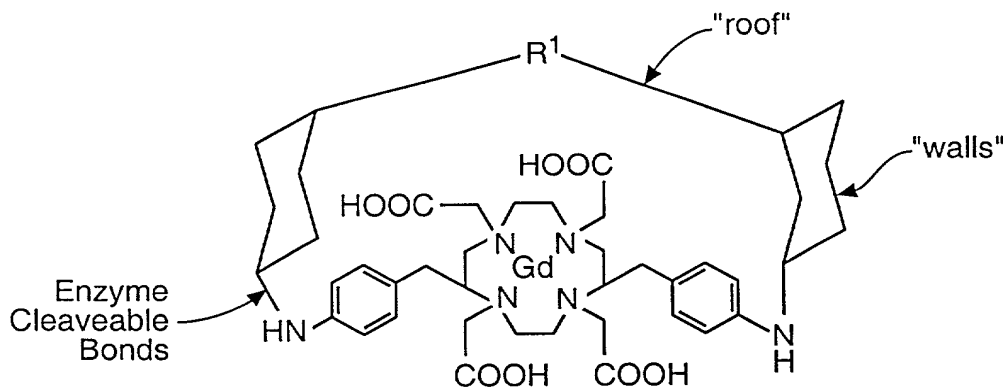


FIG._2

+

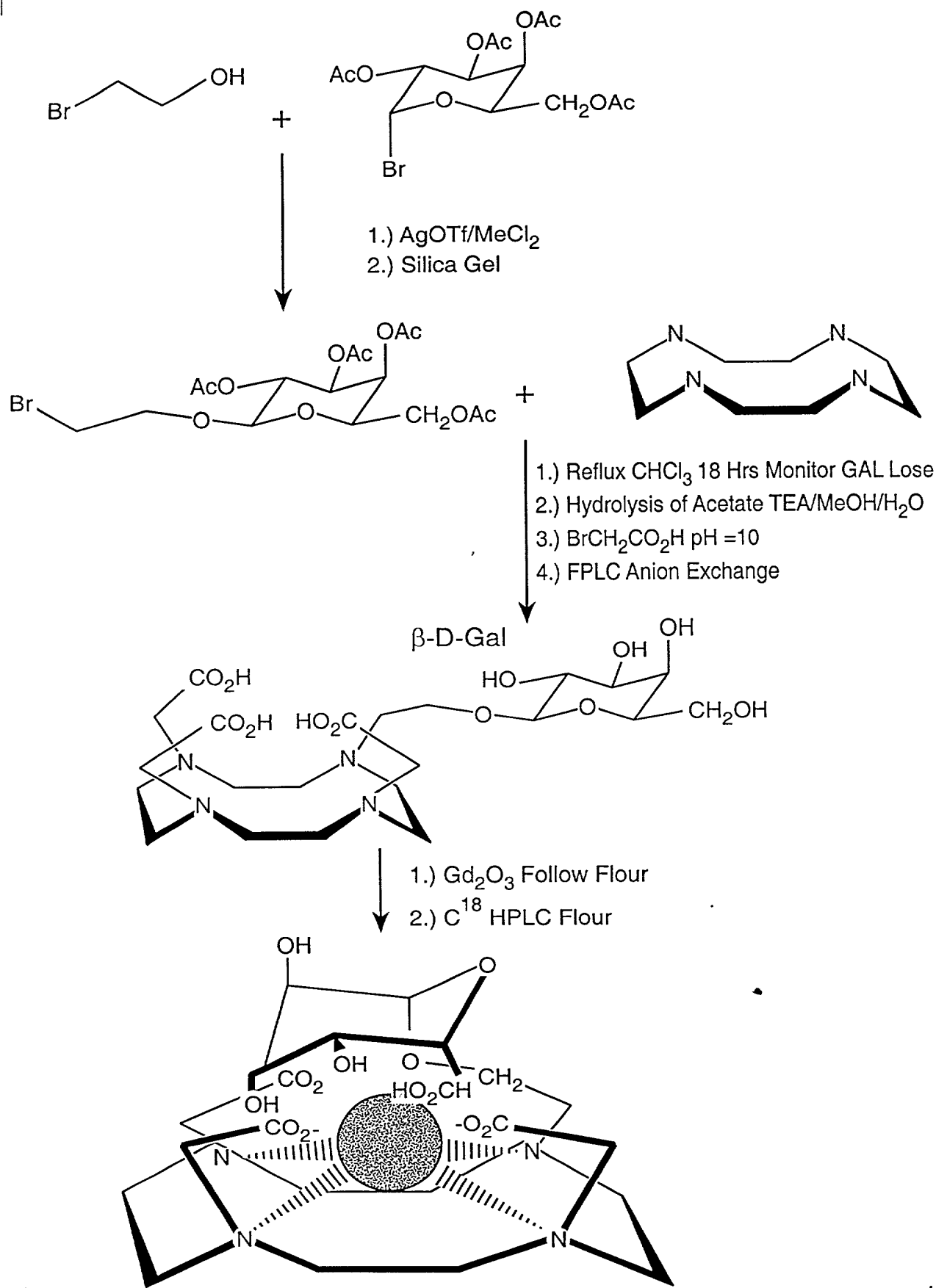
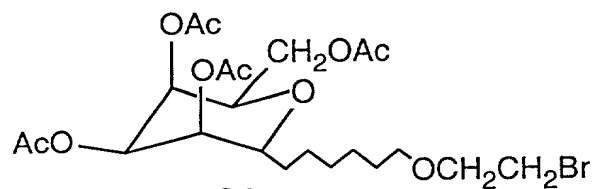
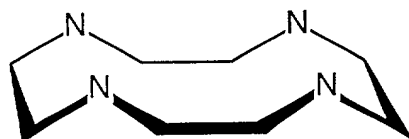
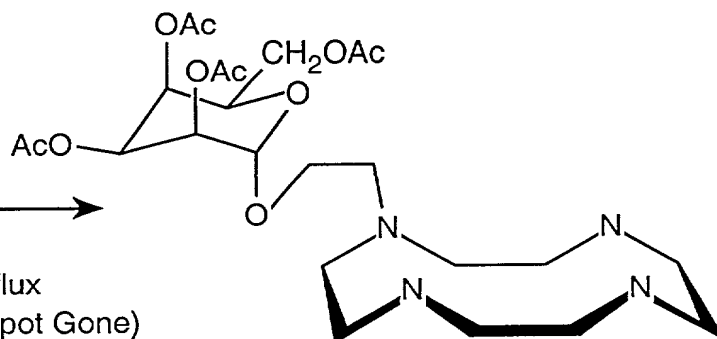


FIG._3

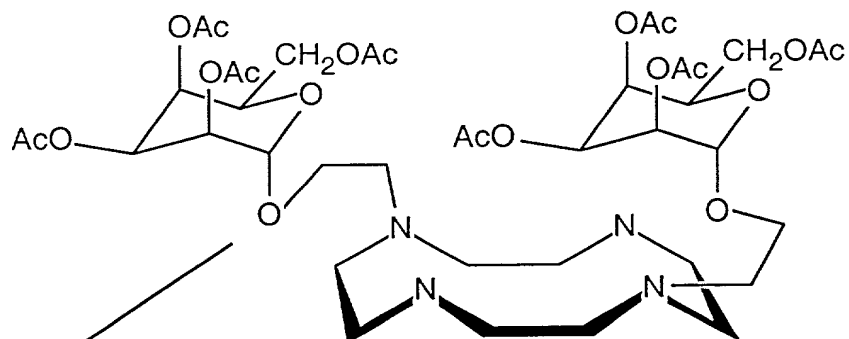


1 + 2

CHCl_3
 48 Hrs Reflux
 T.L.C. (2 Spot Gone)



1



~2:1 6:5

Silica
 4:1 $\text{CHCl}_3/\text{MeOH}$

8

- 1.) Hydrolysis Of Acetate
TCA/MeOH / H_2O
- 2.) $\text{BrCH}_2\text{CO}_2\text{H}$ pH = 10
- 3.) FPLC Cation Exchange
pH = 2 Acetic Acid Gradient

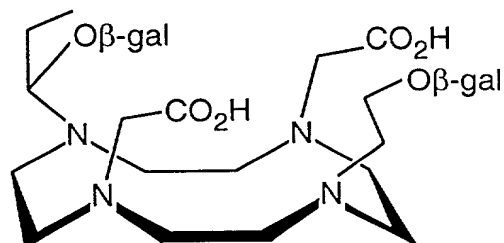
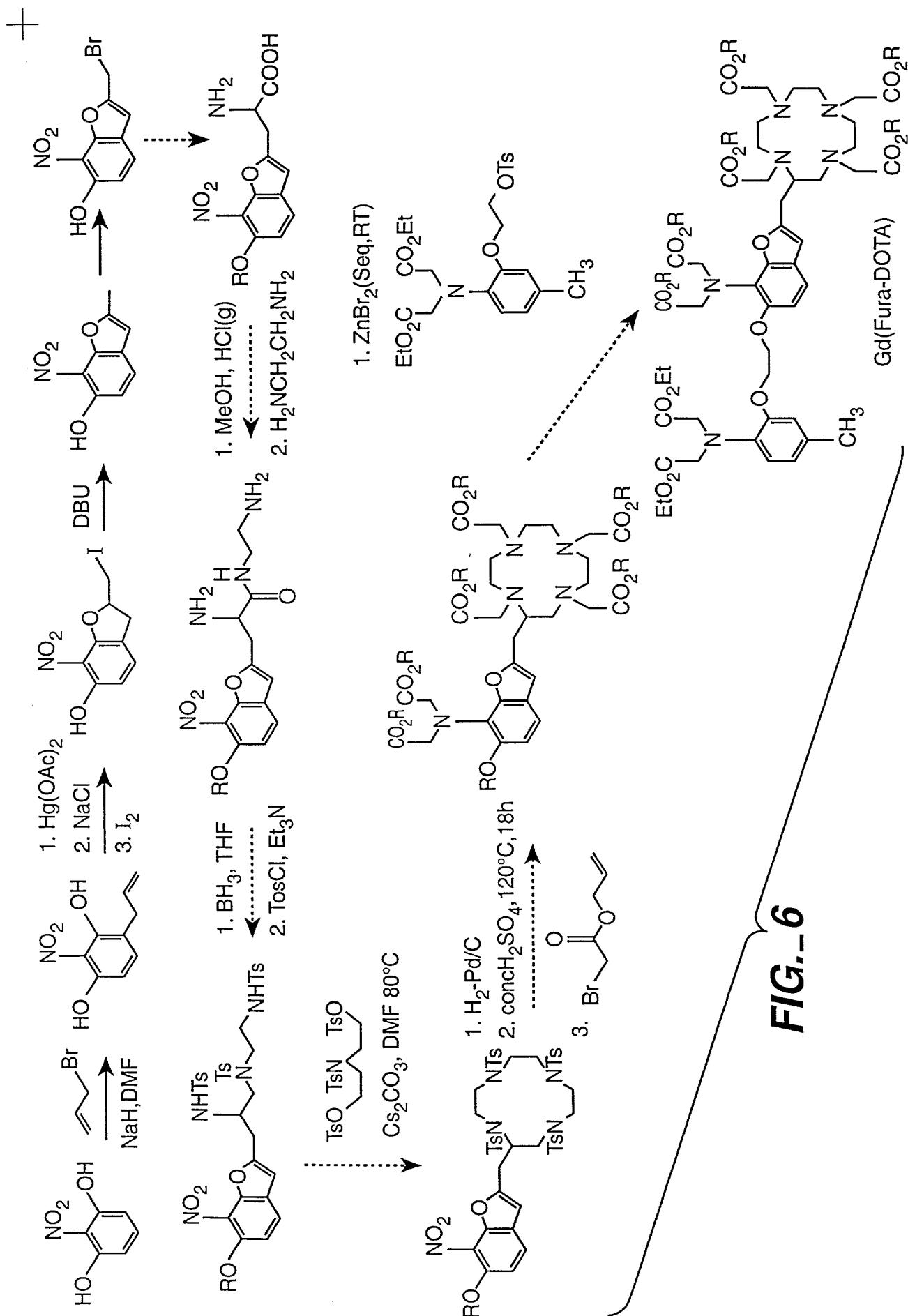
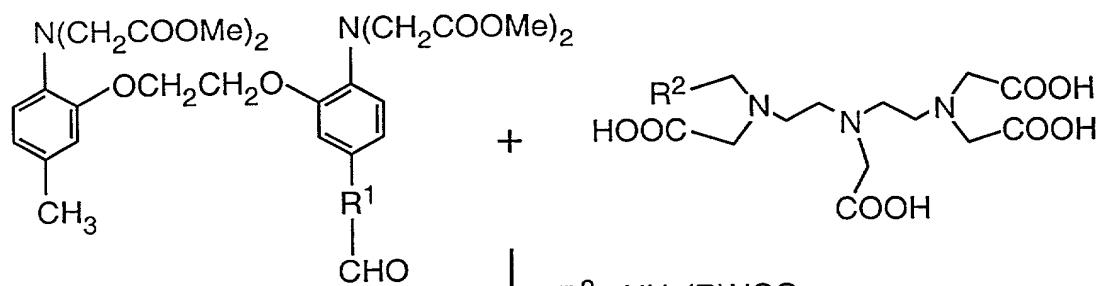


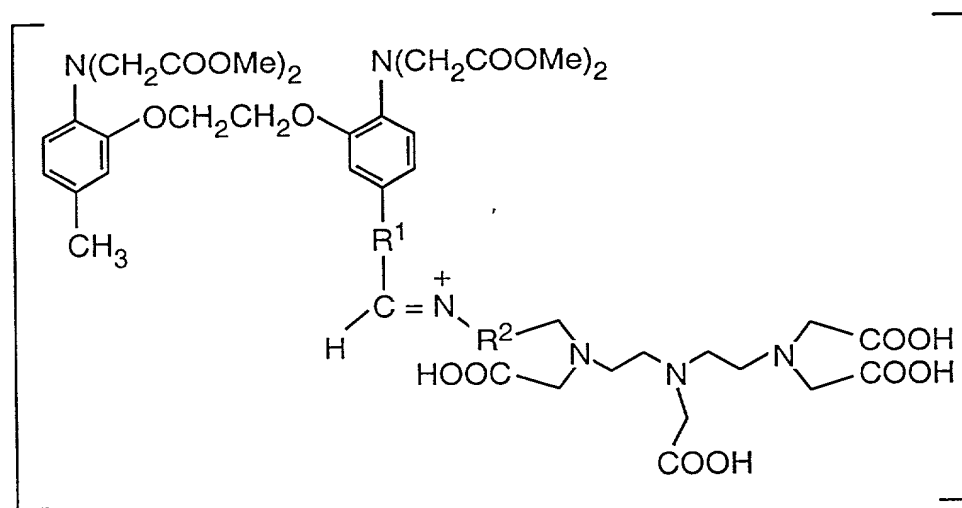
FIG._4





$\text{R}^2 = \text{NH}_2(\text{R})\text{NCO}$

NaCNBH_3



Rearrangement
 HPLC
 Gd(III)

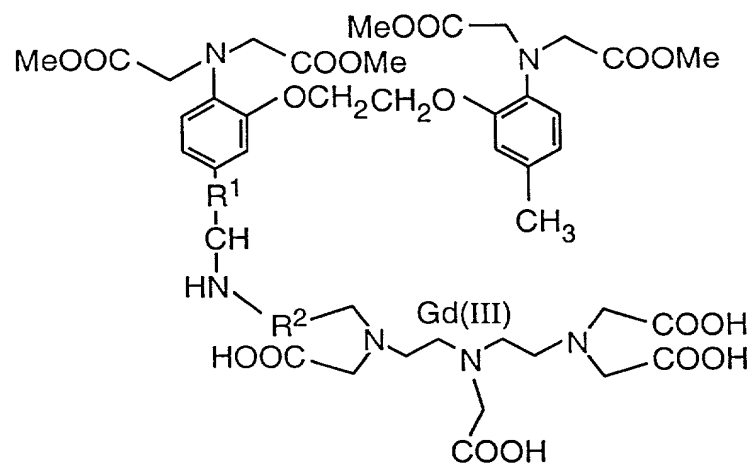


FIG. 7

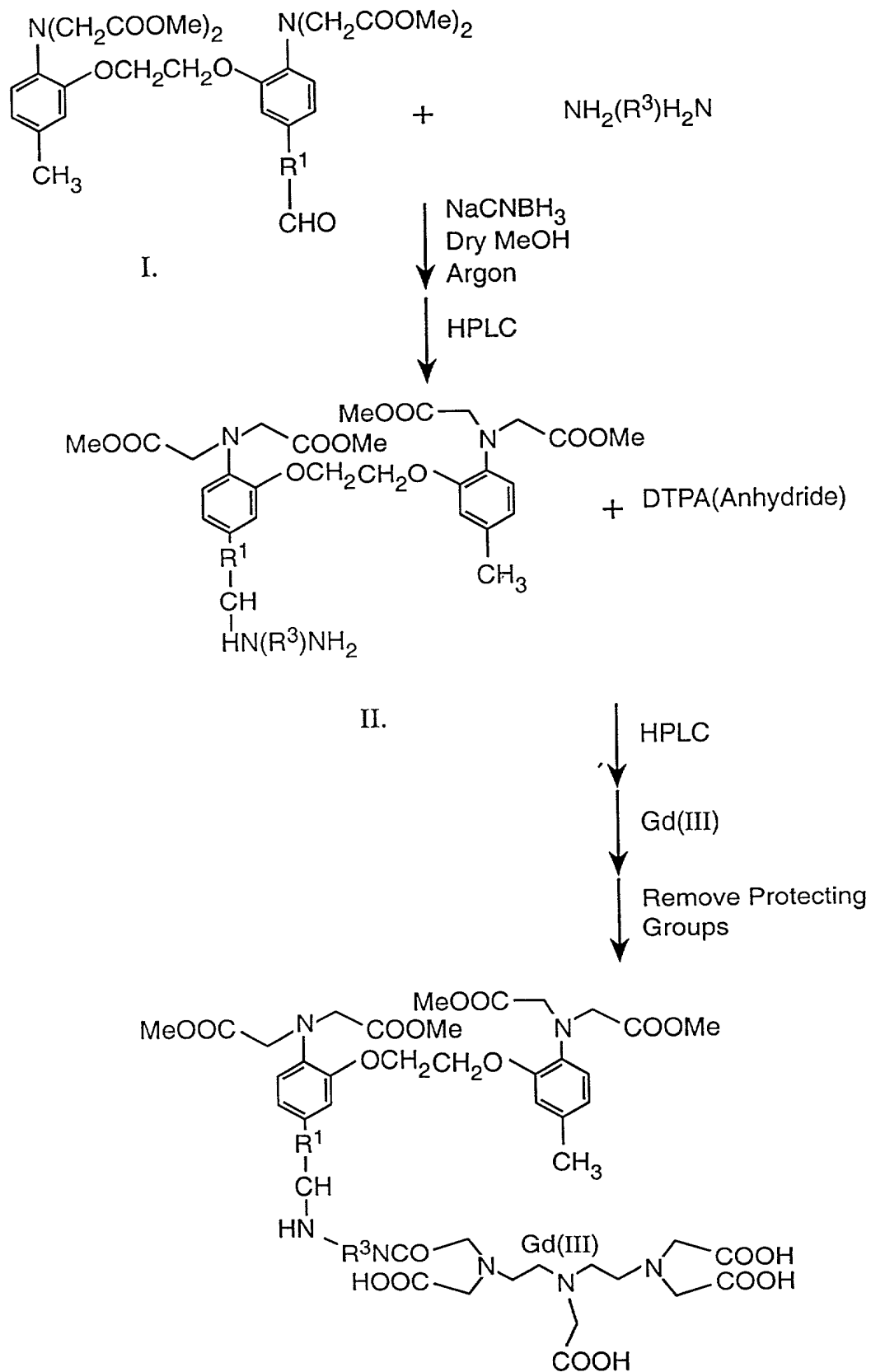


FIG. 8

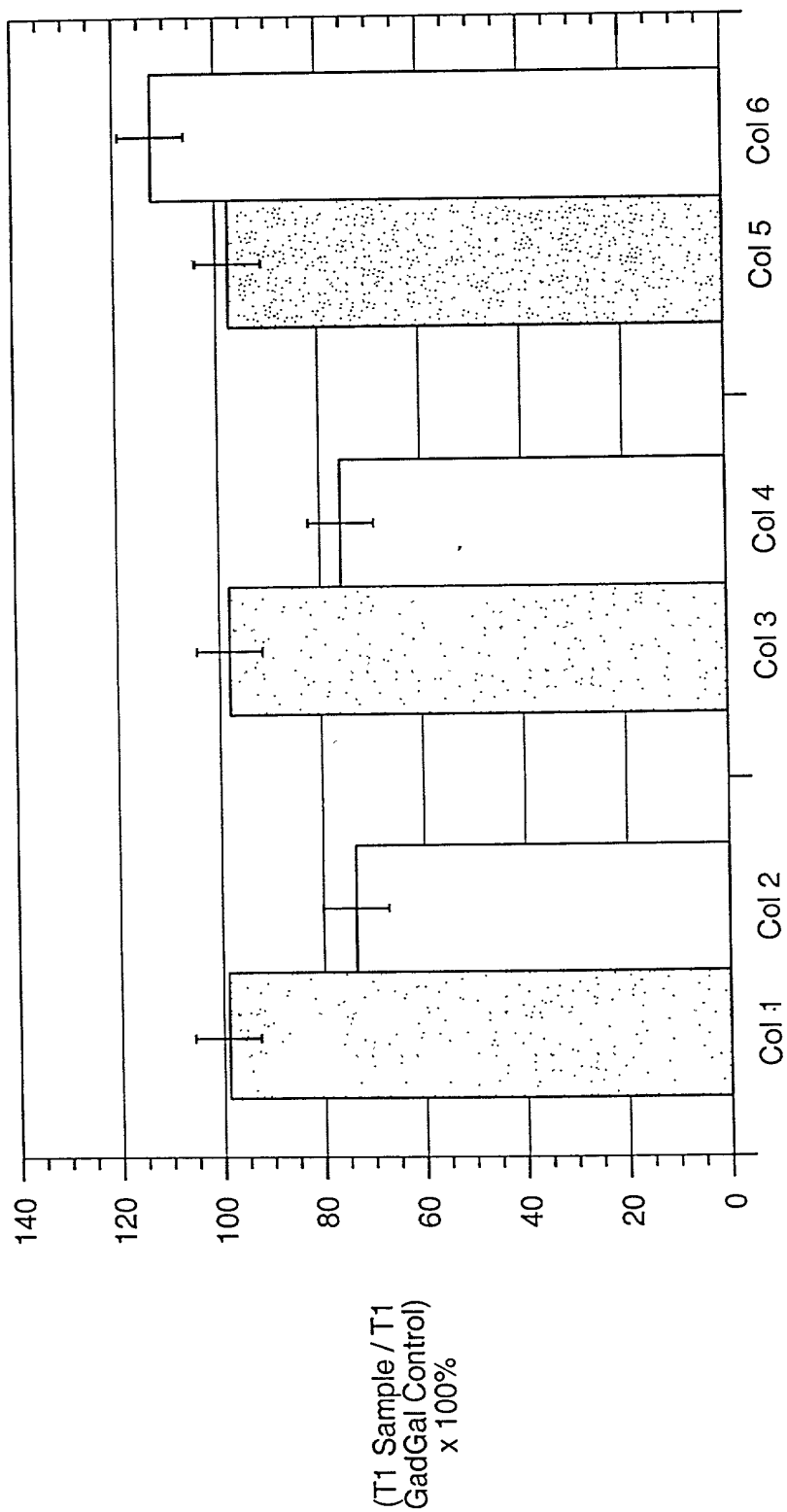


FIG. 9

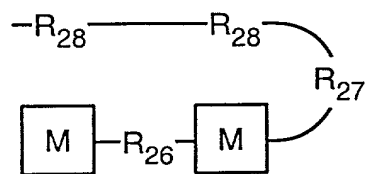


FIG. 10A

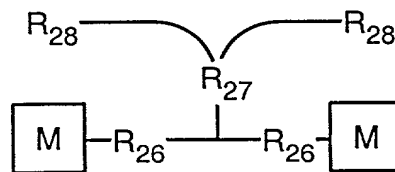


FIG. 10B

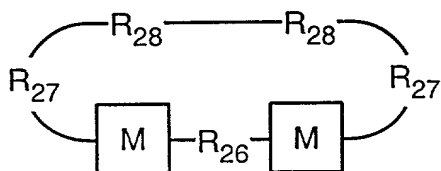


FIG. 10C

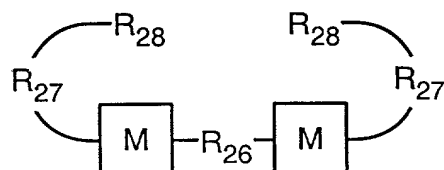


FIG. 10D

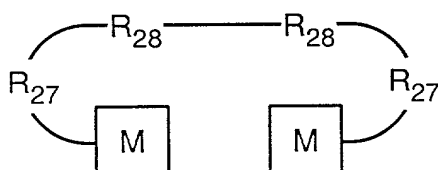


FIG. 10E

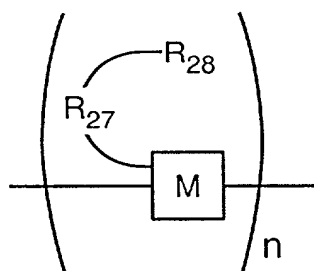


FIG. 10F

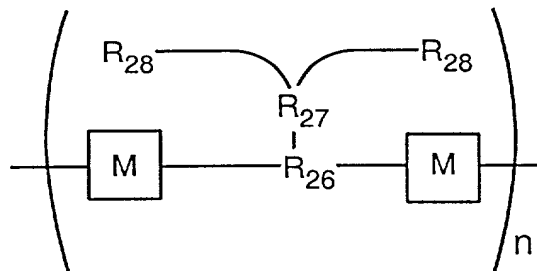


FIG. 10G

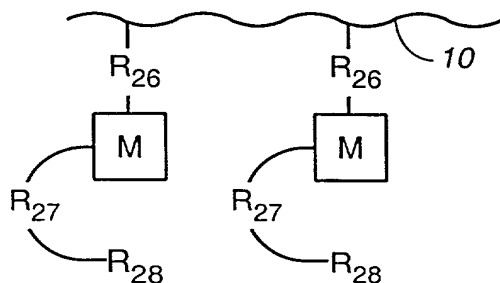


FIG. 10H

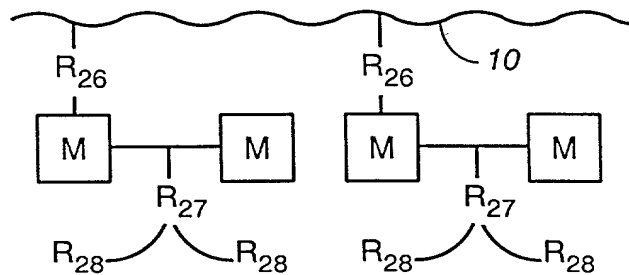
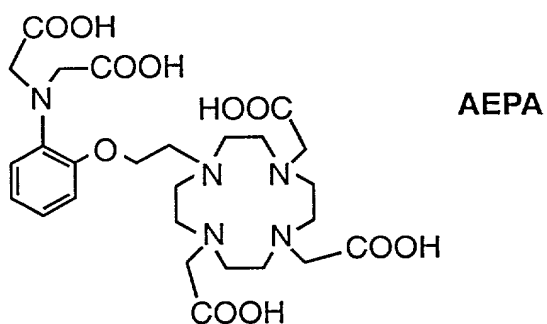


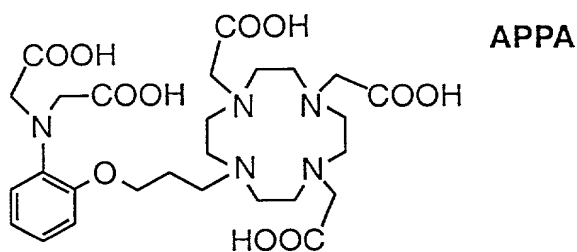
FIG. 10I

+



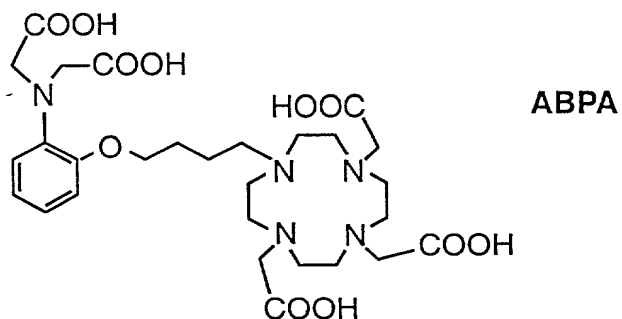
1-o-aminophenoxy-2-(cyclen)ethane-N,N,N',N'',N'''-pentaacetic acid

FIG._11A



1-o-aminophenoxy-3-(cyclen)propane-N,N,N',N'',N'''-pentaacetic acid

FIG._11B



1-o-aminophenoxy-4-(cyclen)butane-N,N,N',N'',N'''-pentaacetic acid

FIG._11C

+

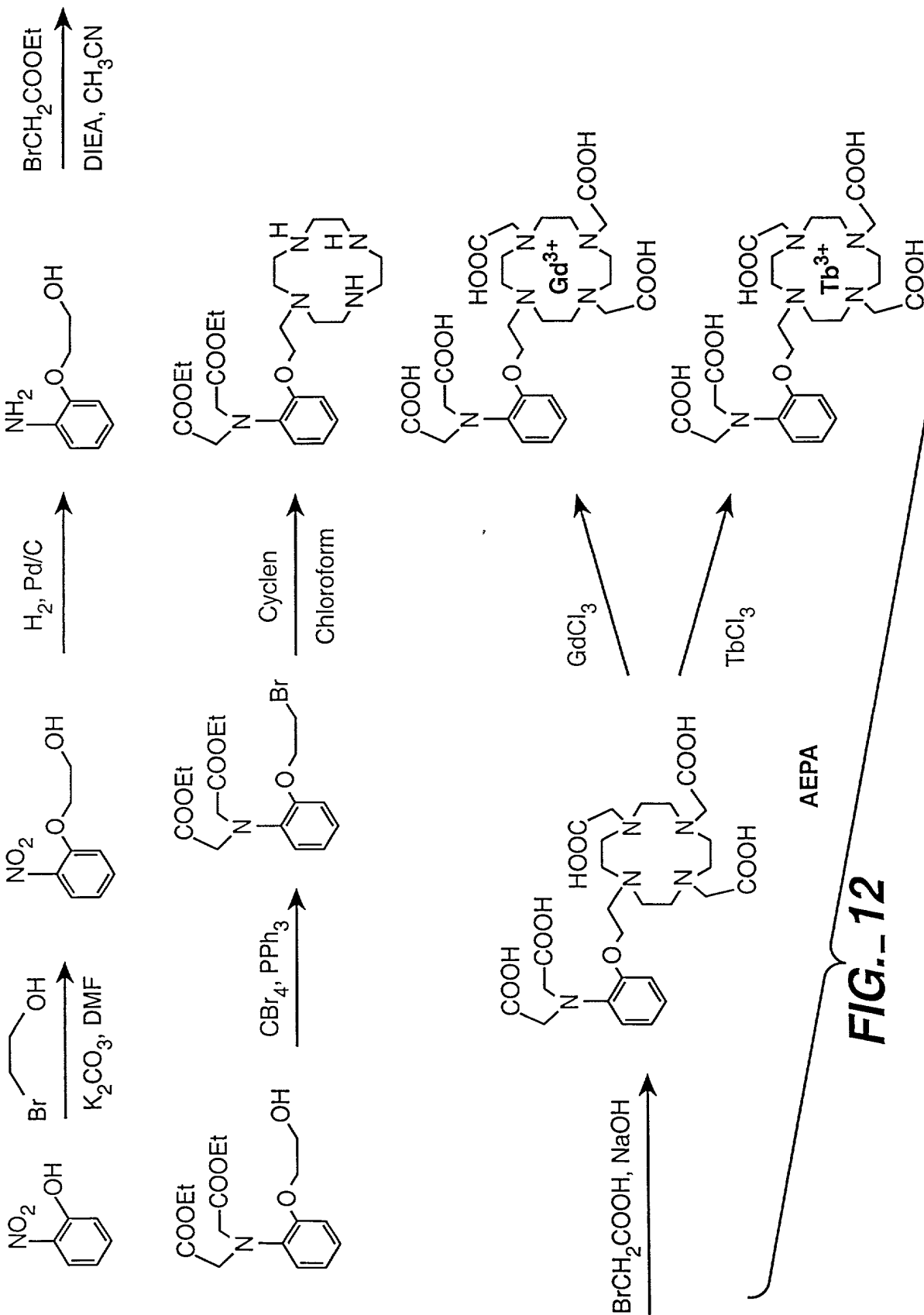
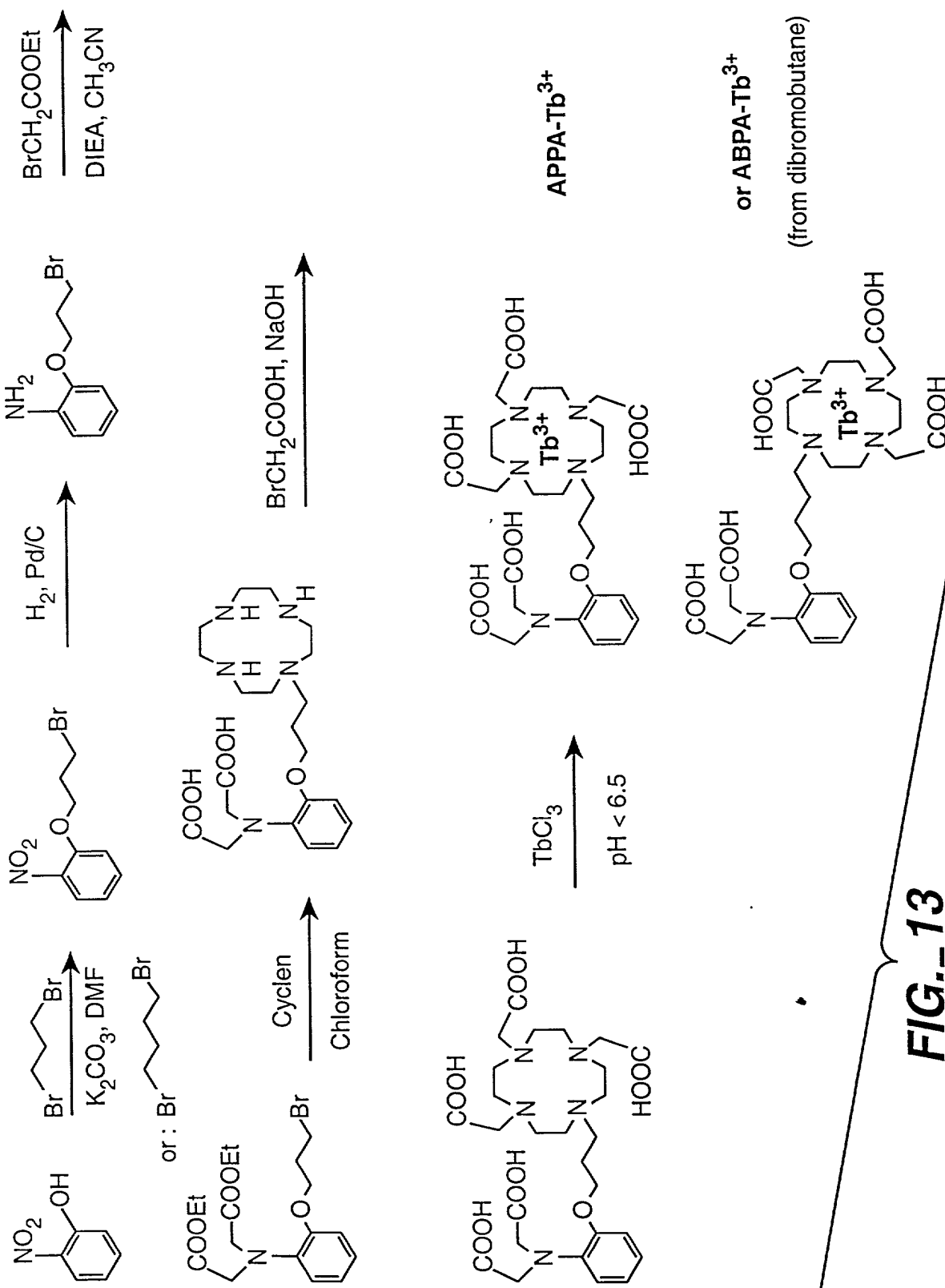
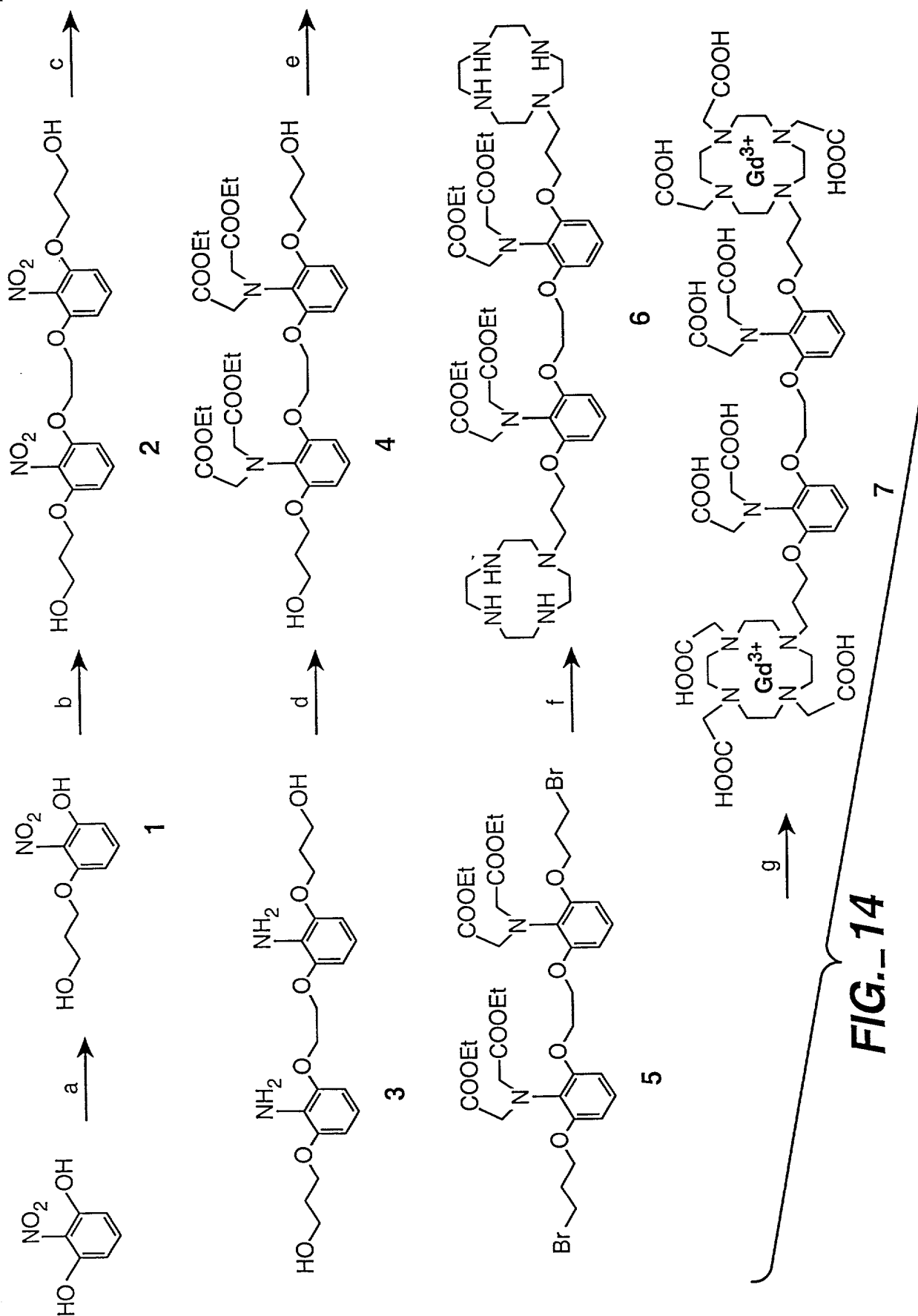


FIG. 12



+



+

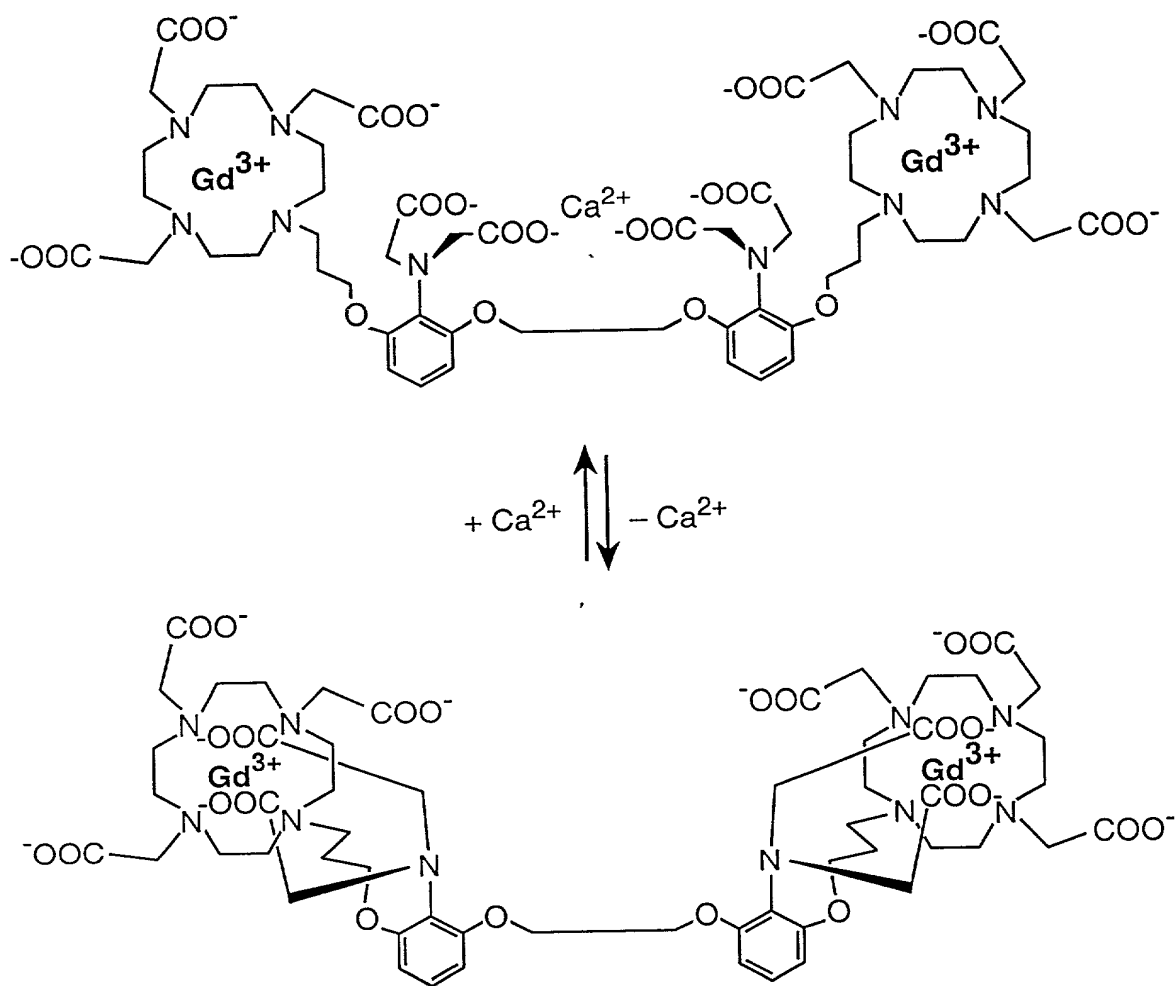


FIG. 15

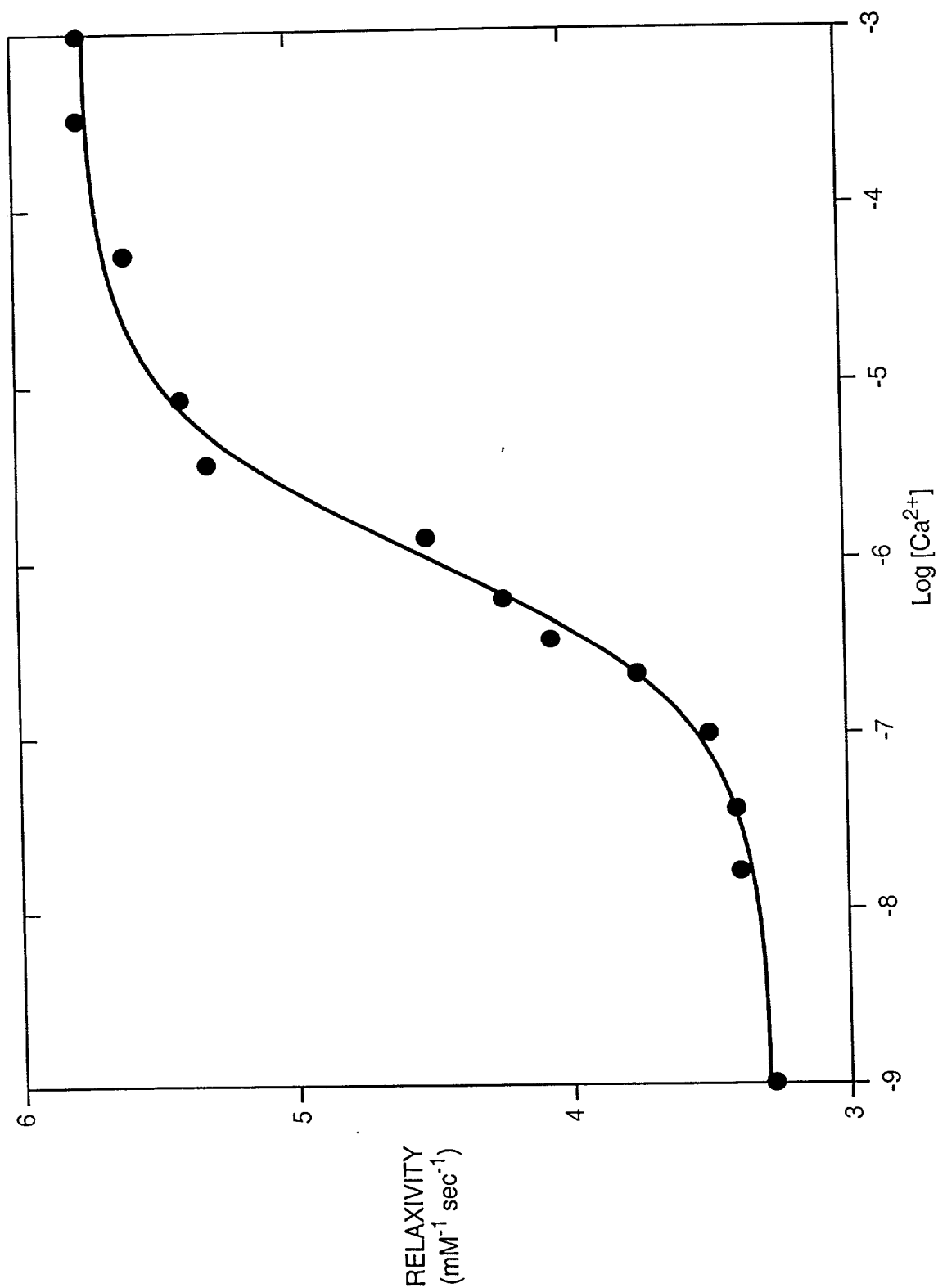


FIG. 16

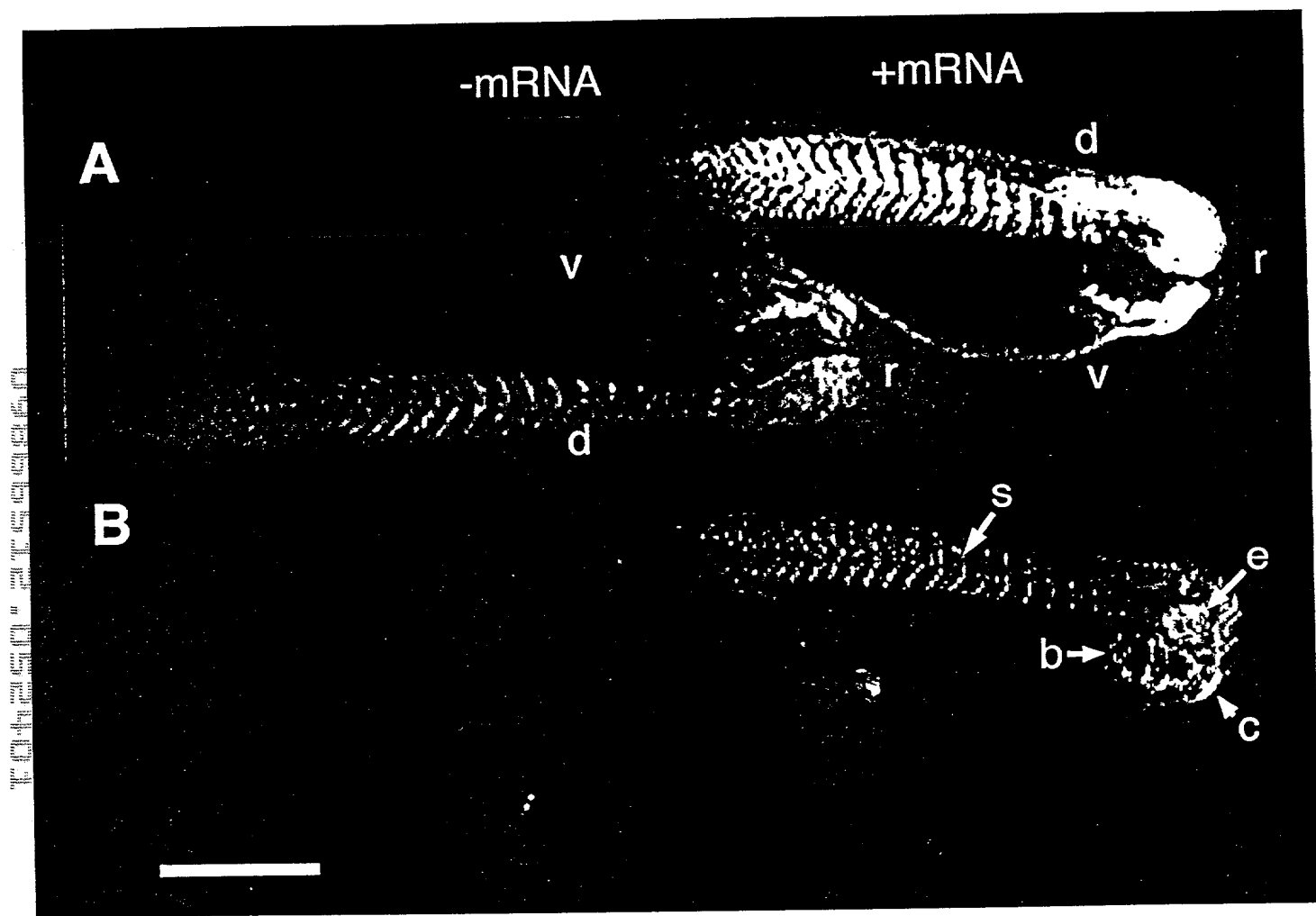


FIG._17

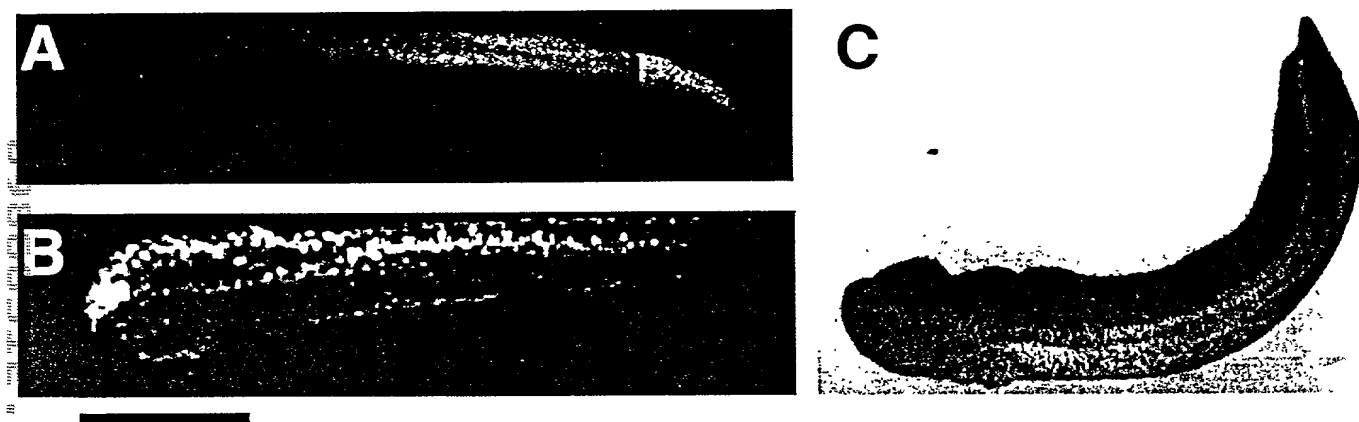


FIG._18

0986512-052401

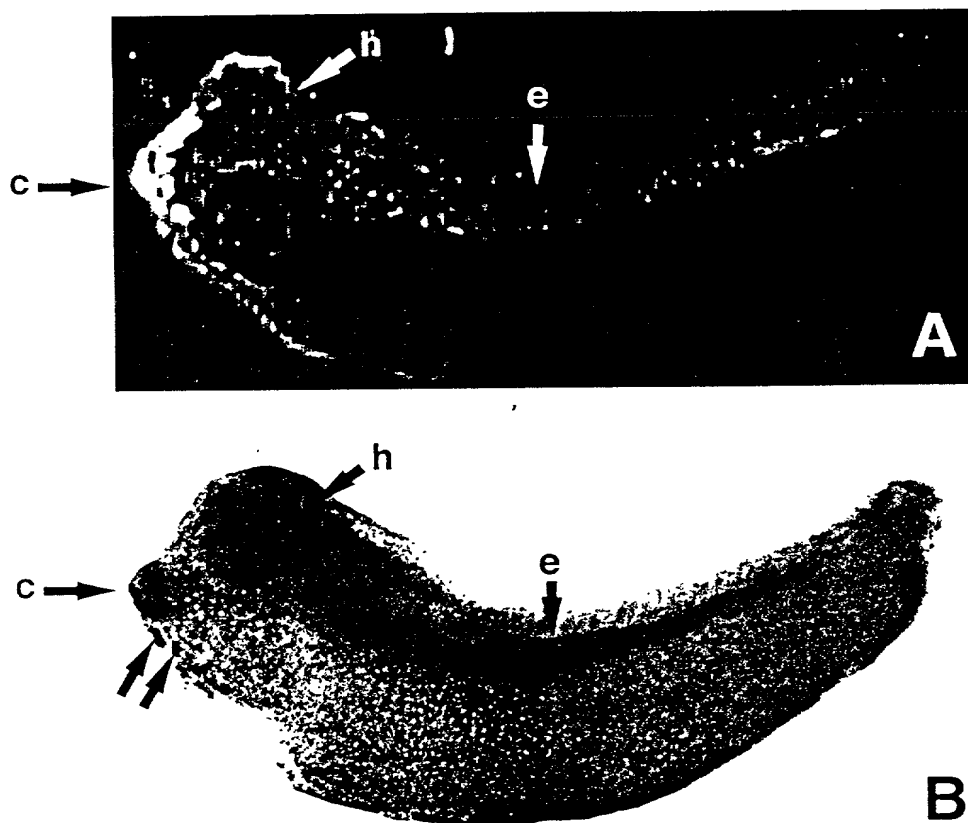


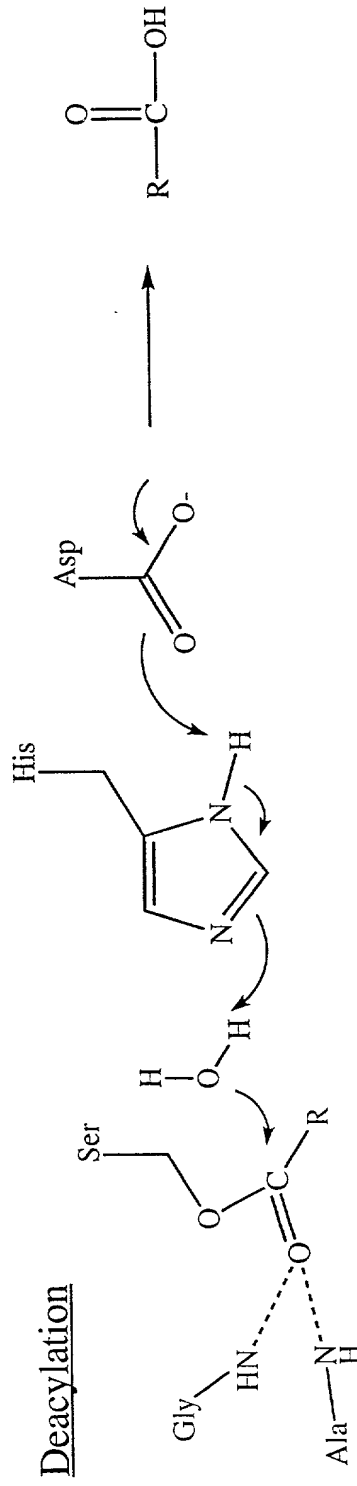
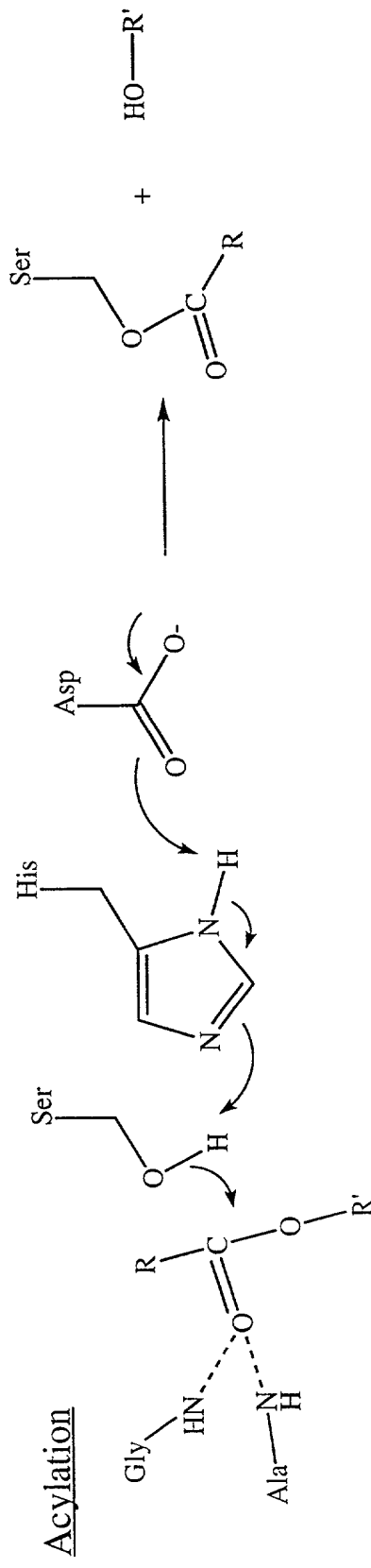
FIG._19

Properties of Carboxylesterases:

1. Efficient cleavage of Ester functional groups

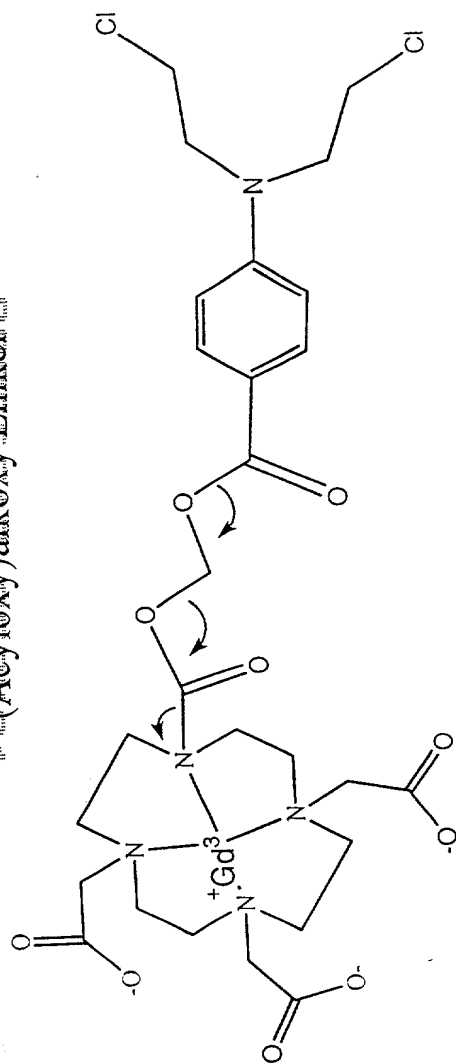


2. Belongs to the family of Ser-His-Asp active site enzymes (serine protease)

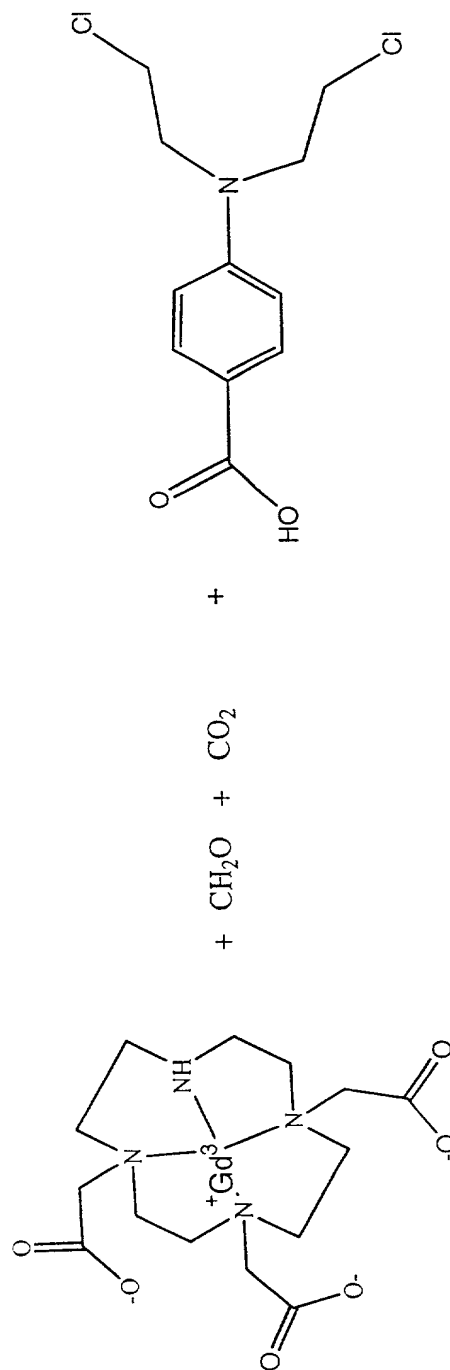


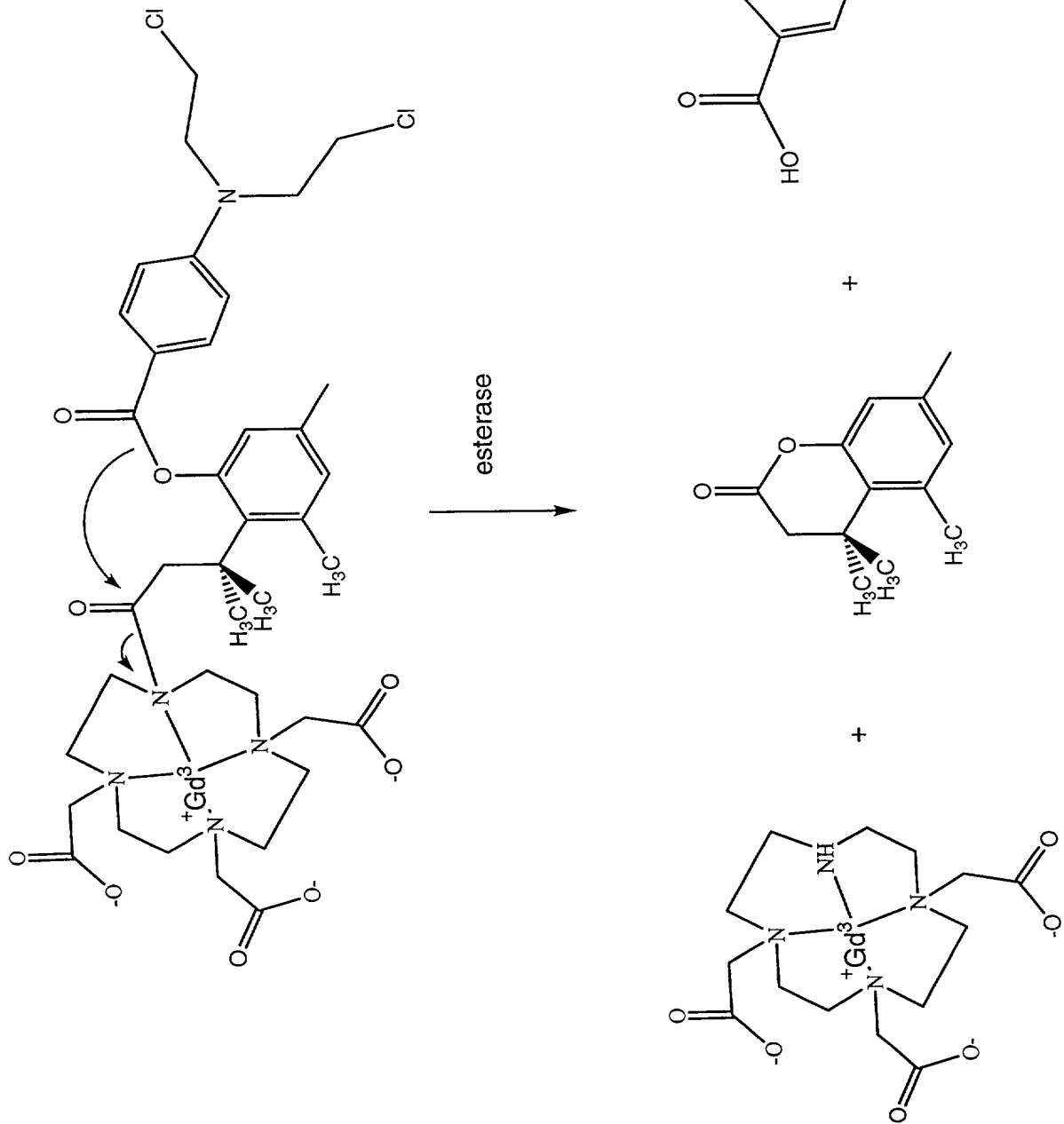
1. ((Acetoxy)alkoxy)Linker

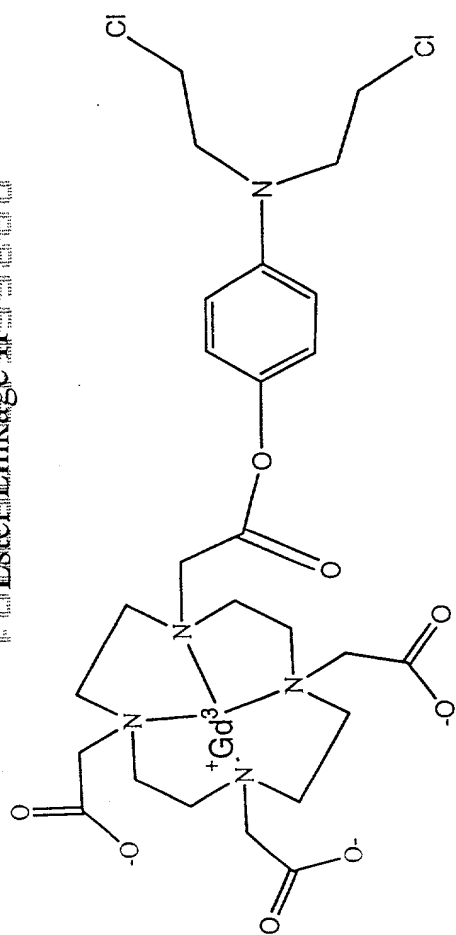
Fig 20A.B



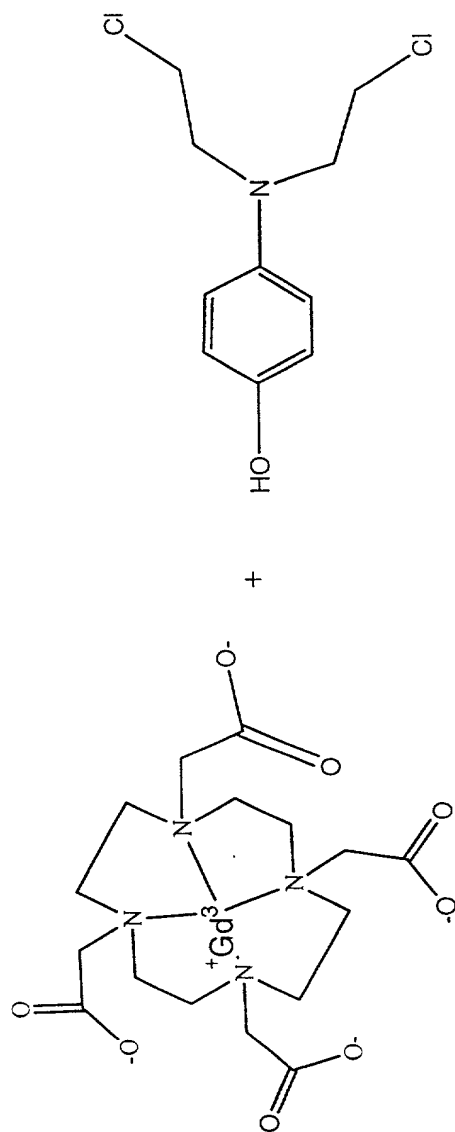
esterase

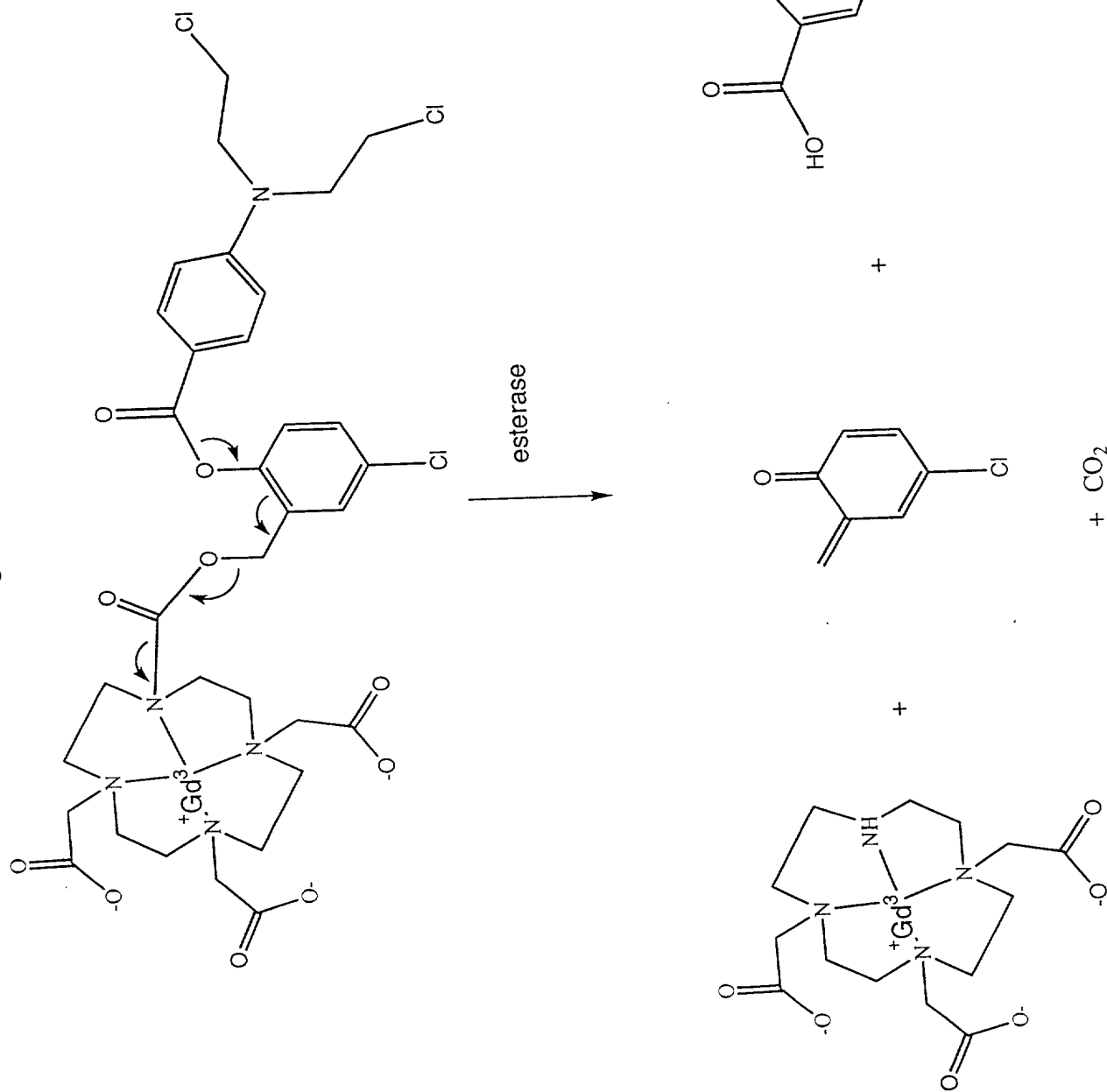






esterase





Fmoc Chemistry for Synthesis of Linker-peptide unit

I.

MBHA Rink Amide Resin

or

PAL-PEG-PS Resin

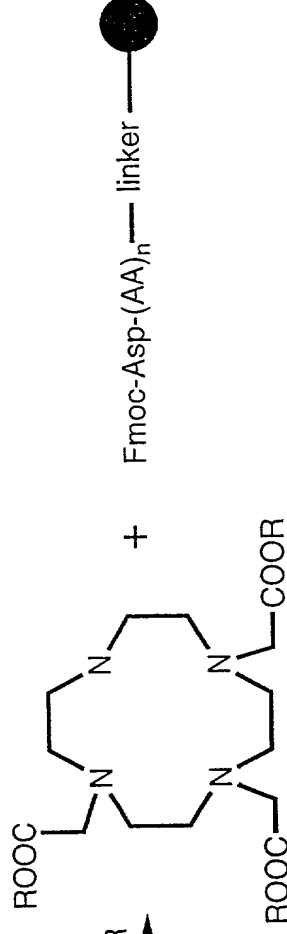
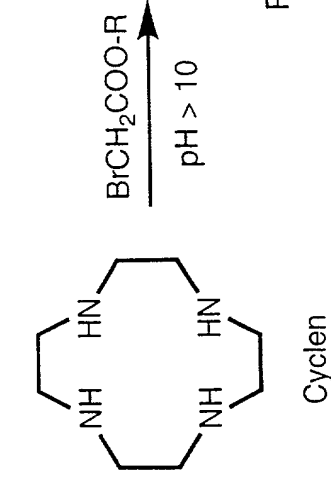
Activation with 20% piperidine
in DMF



Fmoc AA-OH/HOAt/HATU/DIEA

1. N-ε-Fmoc-ε-amino-R acid
[H₂C(CH₂)_x-NH-Fmoc]
2. Fmoc-AA-OH
3. Fmoc-AA-OH
4. (Fmoc-AA-OH)_n
5. Fmoc-Asp-OH

II.



III.

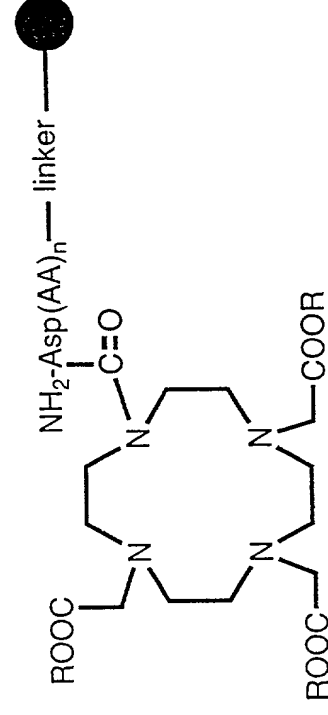
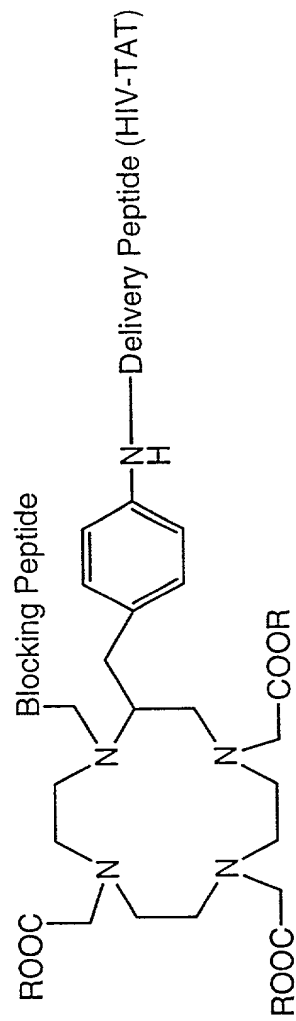


Fig 22

US 2005/0155000 A1



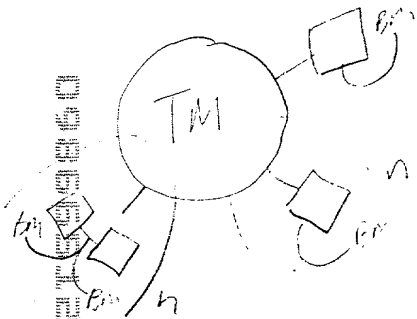
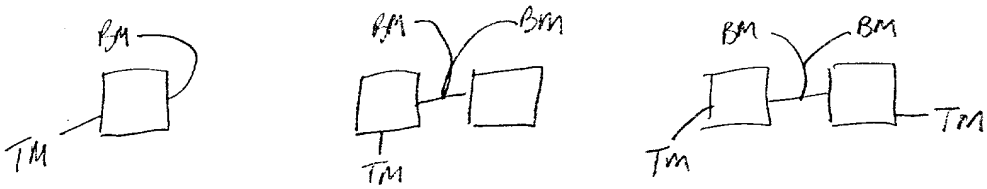


Fig 23